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# RADIUM

EDITED BY  
CHARLES H. VIOL, Ph. D.  
AND  
WILLIAM H. CAMERON, M. D.

VOL. XVI

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No. 1

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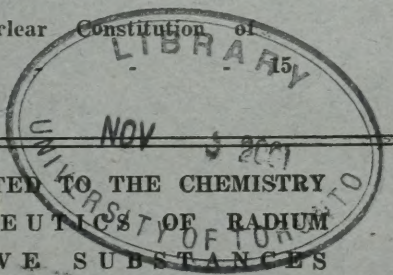
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A MONTHLY JOURNAL DEVOTED TO THE CHEMISTRY  
PHYSICS AND THERAPEUTICS OF RADIUM  
AND RADIO-ACTIVE SUBSTANCES







# RADIUM

A MONTHLY JOURNAL DEVOTED TO THE CHEMISTRY, PHYSICS AND  
THERAPEUTICS OF RADIUM AND RADIO-ACTIVE SUBSTANCES

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Edited and Published by Charles H. Viol, Ph. D., and William H. Cameron, M. D.  
with the assistance of collaborators working in the fields of  
Radiochemistry, Radioactivity and Radiumtherapy.

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## THE MANCHESTER AND DISTRICT RADIUM INSTITUTE, THE ROYAL INFIRMARY, MANCHESTER

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A Report of the Work from January 1st, 1919, to December 31st, 1919

By ARTHUR BURROWS, M.D., Radiologist

Between January 1st, 1919, and December 31st, 1919, 677 cases have presented themselves at the Manchester and District Radium Institute—an increase of 29 patients over the previous year.

The Physicist reports that 355 emanation plates, 990 emanation tubes, making a total of 1,345, were made during the year.

Fifty-one cases of malignant disease, exclusive of rodent ulcer, were rendered free from symptoms and signs during the course of the year. This represents 11.5 per cent. of the total cancerous cases seen at the institute during the year, or 14.8 per cent. not inclusive of those which come under the heading "too early or abandoned treatment." The true percentage rests between these figures.

The 51 cases consist of 1 of carcinoma of the body of the uterus, 8 of carcinoma of the breast, 19 of carcinoma of the cervix of the uterus, 2 of carcinoma of glands, 1 of carcinoma of the lip, 5 of carcinoma of the mouth and tongue, 7 of carcinoma of the skin, 2 of carcinoma of the vulva, 3 cases of sarcoma, and 3 of endothelioma.

A fuller consideration of the radium treatment of cancer of the mouth and the most recent method for the application of radium is given later in this report.

It will be seen in the second table that 31 cases of carcinoma of the cervix of the uterus are noted under the heading of "too early or abandoned treatment." In a large proportion of these cases the patients have failed to attend for re-examination in spite of the fact that they

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were written for, often several times. This state of things is greatly influenced by the fact that one application of radium to a carcinoma of the cervix of the uterus often stops the pain and discharge which the patients are suffering from, so that they do not think it necessary to attend for re-examination. This is unfortunate as the risk of recurrence of symptoms of the disease after one treatment is very great.

Thirty-eight cases of rodent ulcer were apparently cured in 1919, representing 54.3 of the total cases seen. In addition to these, 14 non-malignant conditions were cured.

The examination of pathological specimens during the year has been carried on by the clinical laboratories of these various hospitals participating in the scheme. In the course of a few weeks this will be done in our own research laboratory.

The greater part of the apparatus ordered for the research laboratory has been obtained, and work has now commenced there.

It is hoped that the contemplated provision of a lighter and more airy radium institute, with beds attached, will come nearer to realization during the ensuing year.

### CLASSIFIED RESULTS

TABLE I.

Well at end of year.....	102
Improved .....	251
Not improved .....	75
Died of their disease.....	11
Not suitable for treatment.....	65
Too early or abandoned treatment.....	139
Prophylaxis .....	34
Total.....	<hr/> 677 <hr/>

The number of cases registered during the year was 677

#### RADIUM TREATMENT OF CARCINOMA OF THE MOUTH

This includes carcinoma of the tongue, floor of mouth, fauces, soft and hard palate, tonsils and pharynx.

Hitherto these have been unsatisfactory cases from the point of view of radium treatment, and this is particularly unfortunate because growths of the tonsil, fauces and palate, owing to their position, become inoperable relatively early.

Most radiologists have been inclined to pass over these cases without extended consideration by stating at once that radium does not give satisfactory results. Until recently this was so, and it was often doubtful whether it was worth while attempting the palliation of cancer of the mouth in spite of the extremely unpleasant features of the disease. Now and again a case rather unexpectedly did well, making radiologists think that there must be some more satisfactory method of applying radium or some unknown factor yet to be discovered.

It seems useful, therefore, to discuss the factors present in cases of cancer in other regions which cause them to react favorably to radium, and the particular methods of application of radium used for their treatment.



TABLE II.

*Classification of Cases.*

Disease.	Abandoned treatment and too early.	Well at end of year.	Improved.	Not Improved.	Died.	Not suitable.	Prophylaxis.	Total.
Carcinomata:								
Anus .....	—	—	3	—	—	—	—	3
Body of uterus...	1	1	—	—	—	—	—	2
Bladder .....	1	—	1	1	—	—	1	4
Breast .....	20	8	26	3	1	13	12	83
Cervix of uterus..	31	19	37	10	1	10	—	108
Glands .....	3	2	5	4	1	5	6	26
Larynx .....	1	—	—	—	—	2	—	3
Lip .....	3	1	1	—	—	—	1	6
Mouth & Tongue	10	5	38	9	—	9	2	73
Ovary .....	—	—	—	—	—	1	—	1
Parotid gland ....	—	—	—	—	1	—	—	1
Rectum .....	2	—	3	7	—	3	1	16
Skin .....	4	7	8	5	—	3	1	28
Thyroid gland ....	—	—	3	—	1	2	—	6
Various .....	7	—	3	2	2	4	1	10
Vulva and Vagina	8	2	4	1	—	5	—	21
Sarcomata .....	8	2	8	5	2	4	6	35
Endotheliomata ....	—	3	3	1	—	—	2	9
Mediastinal Tumor..	3	—	2	2	1	—	—	8
Rodent ulcer .....	7	38	22	3	—	—	—	70
Papillomata of Bladder .....	—	—	1	—	—	—	—	1
Benign tumors .....	4	5	2	—	—	—	—	11
Keloid and vicious cicatrix .....	2	—	10	—	—	—	—	12
Exophthalmic goitre	7	—	32	15	1	1	—	56
Nævus .....	6	1	14	3	—	—	—	24
Hodgkins' disease...	1	—	6	—	—	—	—	7
Chronic. inflamma- tion (Tub. gland)	1	—	4	—	—	—	—	5
Skin diseases .....	1	6	14	3	—	1	—	28
Uterine hæmorrhage	1	2	—	—	—	—	—	3
Various (non-malignant) .....	2	—	1	1	—	2	—	6
Leukoplakia .....	2	—	—	—	—	—	—	2
Total .....	139	102	251	75	11	65	34	677

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Before dealing with specific diseases and regions it is best to dismiss those general considerations already well known which adversely influence radium treatment:—

- (1) Large size of tumors with extensive infiltration.

In the mouth, cancerous growths, if not often large, are frequently widespread, and the induration beneath a small tumor in the tongue is commonly much more extensive even than palpation reveals.

- (2) Deficient blood supply of the tumor.

Carcinoma of the mouth seems usually to form early dense hard nodules and masses, with poor blood supply and a tendency to slough and ulcerate.

- (3) Tumors adherent to and involving bone.

Many cancers of the floor of the mouth early in their development become adherent to and involve bone. This condition always renders growths more difficult to treat by radiation, and was in fact one of the earliest observations made in the treatment of rodent ulcers by x-rays operators. After operation, in carcinoma of the mouth, recurrences adherent to bone are among the commonest.

- (4) The rapid dissemination of a growth.

This is obviously a most important factor in prognosis in any form of treatment, and in relationship to cancer of the mouth secondary glands are commonly formed early and grow rapidly.

- (5) Sepsis.

The persistent purulent and inflammatory condition which sometimes follows radium treatment, often called a "burn," is usually a septic reaction. It cannot be definitely stated to prevent the disappearance of a malignant growth, but it does delay healing, gives the patient much pain, undermines the general health, and prevents a timely repetition of radium treatment. It is difficult, although not impossible, to obtain a clean reaction in the mouth, which is frequently a very dirty cavity when affected by malignant disease. It is hardly worth while producing a painful reaction which does not in time bring about the reduction, healing, or disappearance of a growth.

It is thus shown that taken as a whole carcinoma of the mouth most commonly exhibits those features which makes it difficult to treat, but it must at the same time be noted that in some quite early cases radium treatment has often very little beneficial effect, whereas a good result for a tumor in the same stage might have been expected in many other situations. So that when the above general considerations are put on one side there still appears to have been until recently some innate tendency in mouth carcinomata to resist radium treatment.

In the following consideration of other kinds and locations of malignant growths, the matter will be considered purely from the point of view of the removal of the local tumor. The treatment of secondary deposits is deferred until later, although it is best to point out first that conditions such as good blood and lymphatic supplies with rapid growth are often helpful from the aspect of local treatment, though bad from that of general prognosis.

The conditions which respond best to radium treatment are rodent ulcer, carcinoma of the skin, carcinoma of the breast, carcinoma of the



cervix of the uterus, carcinoma of the body of the uterus, endothelioma of the parotid gland, and sarcoma of the nasopharynx. Not considering for the time being the methods employed in applying radium to these cases, their most noteworthy feature (with two exceptions only) is *accessibility*. The next is, provided the important factors mentioned above are not present, their ability to stand without ill effects very *large doses of radium*. Lastly, in the case of endotheliomata and sarcomata there appears often to be a peculiar local *susceptibility* to radium treatment even though the ultimate results may be no better than those obtained in the treatment of more slowly affected tumors.

It would almost seem as if carcinoma of the cervix of the uterus is particularly responsive to radium treatment, as good results are reported from many varying methods of application.

With the exception of carcinoma of the breast and some sarcomata the above-mentioned tumors on the whole form metastases slowly.

Examples of those growths which do not respond well as a rule to radium are: Carcinoma of the rectum, melanotic sarcoma and carcinoma of the mouth.

The upper part of a cancer of the rectum is often inaccessible; also almost the same treatment as that given for cancer of the cervix of the uterus fails to benefit this condition in a like degree. It would seem that cancer located in the rectum is peculiarly resistant to radium, although there, as in all situations, a successful case occasionally occurs and gives hope.

Melanotic sarcoma from its rapid spread so quickly kills, that, putting on one side the fact that there is little chance of making observations on the effect of radium in the local conditions, at present there is small likelihood of radium being of any value in its treatment. Should an early case of melanotic sarcoma come to the radiologist by any chance, he should at once refer the case to a surgeon.

There remain certain conditions such as cancer of the larynx, œsophagus and bowel which suffer markedly from the evil of inaccessibility. Applications of radium to the surface over these growths are generally of little value. Carcinoma of the œsophagus may sometimes be relieved by passing radium tubes down the œsophagus into the lumen of the growth, but the patient's general condition is usually so bad that frequent manipulations of this kind will only hasten his end. One or two cases of carcinoma of the larynx in Manchester have derived considerable benefit from the introduction of emanation tubes into the growth (not placed against it through a tracheotomy tube), and one was without sign of recurrence for nearly twelve months. Laparotomy in cases of cancer of the bowel will admit of the introduction of radium tubes into the growth. This is worth while if the secondary deposits are not too widespread. One case of cancer of the sigmoid colon had laparotomy performed twice for this purpose and was well until lost sight of nearly twelve months later. Another had had laparotomy performed for carcinoma of the colon by a surgeon who abandoned the operation. The condition grew worse, so an attempt was made to improve it by again opening the abdomen and introducing radium. Benefit followed, and the patient submitted three times to laparotomy for this purpose. In the end she reaped the reward of her endurance and has now been well for over three years.

These cases lead up to the subject of the "knock-out blow." In the last three instances given, the particular necessity of trying to find



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a method of radium treatment and dosage which will not need repetition is obvious, so that the radium treatment of malignant growths in inaccessible places needing a severe operation for their exposure may be undertaken as readily and frequently as the idea of such treatment is now rejected.

**CANCER OF THE MOUTH.** It cannot be confidently stated that the difficulty in carcinoma of the mouth is due to position, because endotheliomata and sarcomata of the palate and tonsil respond very well to the application of radium, and carcinoma of the soft palate and tonsil may perhaps be stated to give better results than elsewhere in the mouth. Nor is the growth as a rule very inaccessible. Radium tubes can be retained in position on the surface of a growth by means of dental wax or be thrust into the substance of the tumor.

From the above considerations it may be assumed that the treatment of carcinoma of the mouth and tongue in a potentially septic cavity is the problem to be dealt with, and our object is to find a treatment which is:—

- (1) A form to which cancer of the tongue and mouth is susceptible.
- (2) A treatment which needs little repetition.
- (3) Clean in its reaction.
- (4) Adequate for the treatment of secondary deposits.

Treatment by the application of superficial plates and tubes does not meet these requirements. The burying of tubes screened by one millimetre of silver or three-tenths of a millimetre of platinum, although better is not satisfactory. Such doses as are given to other growths by this later method produce much sloughing and painful reactions, which often become septic. Reduction of the dose both in quantity and time, although again an improvement, does not seem altogether satisfactory. Moreover the possibility of even stimulating the growth must be borne in mind. Stevenson and Joly's needles (three-tenths mm. of steel thick) seems rather an improvement, but something is still lacking.

Recently there has come from the Memorial Hospital, New York (Dr. Janeway), another method, namely, the burying in the growth of small unscreened emanation tubes, no effort being made to recover the tubes. This treatment is of much greater promise. The reason for this may be as follows.

In the London Radium Institute and Manchester, treatment of carcinoma of the skin, and rodent ulcers (the most successful side of radium treatment) is usually carried out by means of unscreened exposures of radium to the surface of the tumor. Should the deep in-duration be very great and not affected by this treatment, the next procedure is to bury lightly-screened tubes in the deeper parts of the growth. Heavily-screened radium plates applied to the surface may be tried if the above method has failed or before tubes have been introduced, but rarely has this procedure been found to be of much value after the other methods have failed. It is of course frequently possible to cure a rodent ulcer in the early stages by applying heavily-screened radium, but the employment of this method after using unscreened radium is rather a sign of failure.

In this way the question of the value of beta rays arises and it would seem as if beta rays are an important factor in the value of radium. At the same time this explanation of the effects produced by the different methods of application of radium may indicate to some degree the sometimes otherwise inexplicable differences between the action of x-rays



and radium. X-rays (softer gamma-rays) have an obvious advantage in the treatment of wide areas, while radium is often particularly useful and more effective in the treatment of local nodules and tumors. This points to the possibility of the opening up of a wide field of action for the combined use of radium and x-rays, each being used for its own characteristic advantage.

In cancer of the mouth the new American method has so far been the best.

The technique is as follows:—After boiling one or more capillary emanation tubes of a strength of two to eight millicuries, the number of tubes varying with the size of the tumor, they are introduced into the growth by means of a large exploring syringe needle and stilette. The distance between them must never be less than one centimetre, nor must they be placed near to healthy tissue or bone, otherwise a very painful reaction will follow. No attempt is made to remove the tubes unless one projects and is uncomfortable, when it may be taken out twenty-four hours or more after the application.

To prevent sepsis the mouth should be cleansed before the application. If possible when the radium is introduced an effort should be made to remove septic material mechanically and by the application of antiseptics. It is remarkable how little sepsis may effect the result when the small unscreened tubes are used, possibly owing to the greater bactericidal action of the beta-rays.

If the rules for avoiding healthy tissue and bone be observed (it is not always possible) a practically painless reaction will often follow. A slough (usually superficial) may or may not form a week or more after the treatment, but this comes away in four weeks to two months, leaving a clean, healthy, soft or sometimes scarred surface.

It is remarkable to see from the zone of inflammation and slough formation how wide the range of action of these tubes may be.

If adequate dosage be employed it may not be necessary to give a second application, and as a rule in successful cases two or three is a maximum number.

Following these notes are illustrative unpicked early cases treated in Manchester by this method during the last nine months. In several it will be noted that other forms of treatment have been employed first without success, and much better results have followed the burying of the capillary tubes.

It is thus seen that we are getting nearer to the desiderata of radium treatment, namely:—

- (1) A method of application of radium to which cancer of the mouth is susceptible.
- (2) A treatment which needs little repetition and may be painless.
- (3) The element of sepsis is diminished or may not be of much account.

## THE TREATMENT OF METASTASES

Should metastases reach the chest or other distant spots, the case is practically hopeless from the point of view of general prognosis.

## GLANDS IN THE NECK

- (a) Glands with some mobility or a good blood supply, if not too large, may be treated by burying for 6 to 48 hours considerable doses of radium emanation, *i.e.*, tubes of ten to twenty-five millicuries, screened by three-tenths of a millimetre of

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platinum or seven-tenths of silver. This treatment will often remove individual masses, and tubes should in addition be buried along the course of the cervical lymphatics.

- (b) Apparent success from the above treatment should be followed by repeated irradiation of the neck on both sides by radium plates or x-rays.
- (c) In very large or ill-nourished masses too small a dose of radium, buried or superficial, may produce no effect or even stimulate the tumor. Too big a dose may produce sloughing or liquification of the tumor with discomfort to the patient and without ultimate benefit. That is to say, some tumors from their nature size and position will not tolerate a dose of radium sufficient to produce a curative effect with present methods. Repeated small treatments present no advantage.

These facts may be stated in another way, namely, that no question of a maximal or minimal dose arises, as the maximum dose which it is safe to give is not sufficient to produce a curative effect on the tumor. In such cases the only hope, and that a slight one, is to remove surgically so far as can be safely done the main or central mass of the tumor and treat the growth remaining by burying radium tubes in it.

*Case 2495. Female.*—This patient, suffering from carcinoma of the tongue and mouth, came for treatment to the radium institute in March, 1919. She had had pain in the lower jaw and a nodule under the left side of the tongue for three months. On examination a hard swelling could be felt in the left side of the floor of the mouth firmly attached to and invading the lower jaw, the center was ulcerated. No secondary glands were palpable.

On March 15th, 1919, six capillary emanation tubes, each of a strength of four millicuries, were inserted into the growth. The reaction was painless. At the end of April the ulceration healed, leaving only slight thickening at the site of the growth. The condition remained unchanged until July, 1919, when recurrence took place behind the original growth. The patient was again treated in the same manner and had some slight pain during the reaction, but the growth disappeared. In November, 1919, a recurrence took place in the anterior part of the floor of the mouth: this case is still under treatment.

*Case 2662. Male.*—This patient had been suffering from leukoplakia of the buccal cavity for six years. Five years previously a growth had been removed from the region of the right jaw (nature unknown). He had been suffering from soreness of the inside of the left cheek for six months, and at the time of examination had on the inner side of the left cheek a round, hard, button-like patch with deep central ulceration, the induration from which had nearly penetrated the cheek. The growth had resisted all treatment.

In August, 1919, two emanation tubes, one of a strength of fifteen millicuries and one of twenty-one millicuries contained in screens of three-tenths of a millimetre of platinum, were buried in the growth. The treatment did not improve the patient's condition. On September 30th three unscreened emanation tubes, two of a strength of four millicuries and one of eight millicuries, were buried in the tumor. Three days later the tubes were projecting and irritating the tongue. They were removed.

On December 22nd the growth had completely disappeared, leaving only a healthy scar.



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*Case 2891. Male.*—This patient presented himself for treatment on October 30th, 1919. A month previously the anterior third of the tongue and some glands on the left side of the neck had been removed. At the time of the operation the diagnosis of carcinoma was verified by microscopic section. On examination he had a flat ulcerated recurrence along the left side of the floor of the mouth with deep, fixed induration. There was also a large gland in the middle of the scar at the left side of the neck.

Four emanation tubes, each of a strength of four millicuries, were buried in the tumor of the mouth. One of a strength of twelve millicuries contained in a screen of three-tenths of a millimetre of platinum was inserted in the gland in the neck. The reaction was moderately painful, and there was some sloughing. At the end of November the ulceration of the floor of the mouth had healed over and only slight thickening remained. The gland in the neck was unchanged.

*Case 2766. Male.*—In July, 1919, this patient, who was suffering from considerable pain in the mouth, came to the radium institute with a view to radium treatment. There was a deep, irregular ulcer on the left side of the tongue on its under surface. One small portion of the ulcer was adherent to the jaw. No glands were palpable. The diagnosis was verified by microscopical examination.

In July four emanation tubes, each of a strength of fifteen millicuries contained in screens of three-tenths of a millimetre of platinum, were inserted in the growth and left in position for six hours. A well-marked reaction followed the treatment, and when this had settled down there was slight improvement in the condition. In October, however, the growth had again extended, and five emanation tubes, each of a strength of four millicuries, were inserted in the tumor; one came out of its own accord two hours later. A rather painful reaction followed, but at the end of December it had settled down, leaving the patient comfortable. Then the ulceration had healed over, leaving a considerable scarred area in the tongue and some thickening anteriorly and posteriorly. These latter areas are now under treatment.

*Case 2514. Male.*—In October, 1918, this patient had a portion of the tongue removed for carcinoma. Except for some aching of the jaw he remained well until March, 1919, when he came to the radium institute with a view to treatment. He had then an elongated soft, fungating swelling along the left side of the jaw with induration beneath. It was adherent to the jaw. No glands were palpable.

Five unscreened emanation tubes, each of a strength of three millicuries, were buried in the tumor. The reaction was very severe, and the patient had much pain with a considerable amount of sloughing. The jaw remained painful till July of the same year. In December, 1919, the pain had gone and the patient was well, and no sign of growth could be found.

*Case 2496. Male.*—This patient was referred from the venereal department suffering from a growth of the tongue. He gave a twelve months' history of pain and swelling of the tongue. The Wassermann reaction was negative. At the time he presented himself for radium treatment there was a flat growth occupying the posterior two-thirds of the left side of the tongue. It was nodular, ulcerated, and weeping. Beneath it there was considerable induration, but it did not seem to extend very deeply. No glands were palpable. Microscopic section confirmed the diagnosis of carcinoma of the tongue.

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In March, 1919, six unscreened emanation tubes, each of a strength of 2.5 millicuries, were buried in the growth. The reaction was practically painless. In the beginning of May the tumor was considerably smaller and flatter, and the improvement continued for some time. In July eight more unscreened emanation tubes, each of a strength of two millicuries, were inserted in the tumor. The reaction was again painless, and after it had passed off no growth could be palpated, but some scar thickening remained.

The patient has remained in the same condition until the present time—a period of five months.

*Case 2634. Male.*—In May, 1919, this patient was referred to the radium institute with a three months' history of pain in the mouth. On examination a flat ulcerated growth of the left fauces, tonsil and posterior part of the tongue could be seen. There was considerable induration beneath and the growth was considered to be a very advanced one. One gland was palpable in the left submaxillary region.

In June three emanation tubes, each of a strength of eighteen millicuries and screened by five-tenths of a millimetre of platinum, were inserted in the growth for six hours. Very little improvement followed. In the middle of October five unscreened emanation tubes, each of a strength of four millicuries, were buried in the ulcer. A moderately painful reaction followed, but at the beginning of December most of the ulceration had healed, the induration was much diminished, and the pain had gone. The growth is awaiting further treatment.

The histories of other cases treated in a similar manner differ very little from the above examples, showing at least a more or less uniform local success.

A description is given together with three cuts illustrating the apparatus in which, by the use of liquid air, the radium emanation is removed from a radium solution, purified and tubed for therapeutic application.

\* \* \* \*

## RADIUMTHERAPY OF THYROID\*

A. N. CLAGETT, M.D., Chicago, Ill.

In dealing with this subject we shall limit our discussion to the vascular variety of thyroid disease. We have had no experience in treating goiter of the hypothyroid form with radium, in fact, this being a non-functioning form it would seem that any process that would interfere with the blood supply of the gland would be injurious and perhaps accentuate the existing condition. We have treated 31 cases of exophthalmic goiter of varying degrees of severity, the first case being treated in September, 1917. The age of the patients varied from 74 to 16 years. Only two of the patients were young. One as stated 16, the other 19. These were both cases with pronounced exophthalmic symptoms and were not physiological goiters at all. It is known to all of you that the tunica intima of the blood vessels is exceedingly susceptible to the radium ray eventuating in an obliterative endarteritis, also it is well known that a new cell or diseased cell is usually many times more sensitive to radium than an adult cell. Working on these two premises it would seem nat-

\*Reprinted from the *Journal of Radiology*, Vol. 1, Feb., 1920. Read before the Western Roentgen Society, December, 1919.



ural that a growth of great vascularity and containing new growth cells should give reaction if treated with radium. Attempt has been made to ligate more or less of the thyroid arteries to starve the gland into subjection. Surgical attempts have removed a portion of the gland but the former process, of these two, only attacks the blood supply, not the degenerative cells, and the latter process while removing parenchymatous tissues along with the diseased part certainly left behind diseased tissue in the remaining portion, and the blood supply to this part more or less undisturbed. It is consequently only a question of time for there to be further degeneration and more toxic substances poured into the blood streams with further reduction of the normal functioning tissues of the gland. Of the 31 cases that we have treated with radium, six had already been operated with recurrence of symptoms as bad or worse than before. We have had to ray five cases the second time as the dosage was probably inadequate. One patient has taken up Christian Science, apparently not befitted by the treatment; two with very bad broken compensation of the heart have died since treatment from acute dilatation, one 3 months after treatment, the other  $5\frac{1}{2}$  months, though in both cases the pulse had been slowed an average of thirty beats and the nervous symptoms were considerably reduced. In one case out of five there has been no reduction of the goiter. The others have diminished from  $\frac{3}{4}$  of an inch to  $3\frac{1}{4}$  inches in circumference. One woman patient, age 35, was burnt, the burn healing in twenty-four days and leaving a white scar the size of a nickel on her neck. Her goiter also did not go down until thirteen months had elapsed and suddenly the neck circumference diminished  $1\frac{3}{8}$  inches in a space less than two months.. There has been symptomatic cure in all of these cases with the exceptions noted. The pulse beat has usually been reduced twenty to fifty beats, the nervous symptoms and tremor have vanished; exophthalmos has become less marked or disappeared entirely; patients have gained in weight and general well being. Certainly how permanent this will be we do not yet know, as our first case dates back only about twenty-seven months and thirteen cases have been treated during this present year.

At the risk of being somewhat tedious, we shall describe in detail the technic employed, having observed that the articles written and published appertaining to radium treatment contain a vast amount of information as to what is being done but with practically no information as to how the man did it, and that would seem to be quite essential, if it be published with a desire to be helpful. We first rayed goiters in this manner. We divided the neck area into rectangles  $1\frac{1}{2} \times 3\frac{3}{4}$  of an inch dimension. We placed upon each square a radium tube containing 25 milligrams of radium element screened with a  $\frac{1}{2}$  millimeter of silver, one millimeter of brass and two millimeters of para rubber and left in situ for two hours. The whole goiter was covered in this manner. We found that there was considerable hyperemia of the skin, a few cases taking on a bluish appearance apparently suggestive of a burn though this did not take place. The action on the goiter was effective but it seemed that too much action was wasted upon the skin, so we manufactured a lead cone open at the bottom and the top, the sides composed of lead 3 millimeters in thickness—the bottom of the cone  $2\frac{1}{4}$  inches square, the top 1 inch. Two thicknesses of rubber glove were placed over the bottom of the cone; it was then stuffed with cotton until an altitude of 1 inch was attained and then 100 milligrams of radium element placed

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upon this, using  $\frac{1}{2}$  millimeter of platinum and 1 millimeter of lead and the top then covered with cotton, lead and adhesive plaster. The average neck can be treated with two applications of the cone. A line is drawn down the center of the neck, other lines on each side of this  $\frac{1}{4}$  of an inch away and then a square is marked out with indelible pencil so that when the cone is placed upon the tumor the lines are just visible all around. In some of the larger goiters it has been necessary to map out three squares, one over the isthmus and one over each lobe. The cone is strapped in place with adhesive plaster and usually left for six hours on each square. In a few of the more exaggerated conditions we have increased this exposure up to twelve hours and we have noted that there is scarcely a reddening of the skin but there seems to be most efficient action given by the gamma ray upon the thyroid tissue. Usually these patients seem a little worse for the first few days or week due to some edema of the gland but after about two weeks, improvement begins and at the end of a month the improvement is decided.

We would simply say in closing, that eleven cases in our series of thirty-one had been declined as operable risks by some of the best surgeons in the country and that these patients, several of them wives, sisters and aunts of physicians are now enjoying good health and attending to their regular duties.

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## REVIEWS AND ABSTRACTS

Ruth C. Theis and Halsey J. Bagg. The Effect of Intravenous Injections of Active Deposit of Radium on Metabolism in the Dog. *Journal of Biol. Chem.*, XLI, 525-535, April, 1920.

"There have been few experiments reported on the effect of radium on normal metabolism. . . Berg and Welker have studied the effect of radium salts upon the metabolism of dogs. The doses employed were very small, but these investigators concluded that ingestion of radium *per os* was followed by a stimulation of the catabolic processes as indicated by a slightly increased output of nitrogen in the urine. An increased volume of urine was also noted."

"In experiments where radium salt is given, it is obvious that one cannot be certain whether the effects noted are due to the element radium or the rays emitted by the element."

"The present work has been planned to study the effect of the active rays upon the general metabolism of the dog. Solutions of sodium chloride which contained active deposit from radium emanation were used. To prepare the solutions, sodium chloride is first dried and packed into a bulb and left in contact with radium emanation for 3 or 4 hours. The emanation is then pumped off and the salt dissolved in water in such concentration as to give a solution isotonic with the blood. The solution is drawn into a syringe and the amount of activity determined by a gamma ray instrument. After the injection, the radioactivity remaining in the syringe is again determined and the amount injected computed by difference. The radioactivity is expressed in millicuries. It should be noted that the number of millicuries injected cannot be controlled exactly as an irregular quantity (25 to 50 per cent) will remain in the syringe. The rapid decay of the active deposit introduces a second source of error



in estimating the quantity injected. Radium A decays completely within 15 minutes after the preparation of the solutions. Since our injections were made after 15 minutes, only Radium C need be taken into account. Radium C falls to 3 per cent. of its initial value within 3 hours, so that the physiological activity of the injected solution can last only a relatively short time. The physiological effects are presumably due to the alpha radiation."

"Two animals were employed in the experiments described below. Dog 1 was a Dalmatian female of about 15 kilos. Benedict has shown that this breed of dog regularly excretes large amounts of uric acid. We therefore used a Dalmatian in order to bring out any possible effect of the emanation upon the metabolism of this substance. Dog 2 was a bull-terrier female of about 12 kilos. Each animal was kept in a metal metabolism cage constructed for the proper separation and collection of urine and feces."

"The diets employed for both dogs were made up of cracker meal, dog biscuit, evaporated milk, bone ash, and (in the case of Dog 2) a little casein. Dog 1 received 6 gm. of nitrogen and about 1,000 calories per day; Dog 2 received 5 gm. of nitrogen and about 660 calories per day."

"Experiments with the Dalmatian dog—The first 6 days (February 28 to March 5) serve as the control period before the first injection. On March 5 the dog received an intravenous injection of 95 millicuries of the active deposit. On the day of the injection there seemed to be no effects on the general condition of the animal but on the 2 following days the dog had to be coaxed to eat the food and the feces were softer than usual. After this no further general effects were present. An examination of the nitrogen partition shows a sharp rise in the total nitrogen output, which reaches its maximum on the 2nd day after the injection. This increased nitrogen is distributed among all the nitrogen constituents except creatinine. Ammonia increases proportionately more than does urea. Indeed the increase in the ammonia suggests a definite acidosis. The uric acid increases by about 50 per cent. over that of the preliminary period. It is possible that this is associated with the destruction of white blood corpuscles which follows the injection. Phosphates and urinary volume both tend to show definite increases over the preliminary period."

"The total nitrogen remains high for 5 days after the injection, and then drops suddenly. The ammonia and particularly the uric acid drop more slowly. The latter does not reach the level of the preliminary period until 12 days after the injection."

"On April 4 the dog received a second intravenous injection of 30 millicuries of the active deposit. This dose is scarcely a third of the quantity given in the preceding experiment. The total nitrogen again increases, and again the maximal figure is reached on the 2nd day after the injection. The small dose employed in this experiment is followed by only a slight and transitory rise in uric acid. On the 3rd and 4th days after the injection creatinine shows an increase well above the preliminary period."

"On April 15 the dog received its third injection of the active deposit. On this day 42 millicuries were given. This injection is followed by a marked and prolonged effect. Total nitrogen, urea, and ammonia increase and remain high for almost 2 weeks. Creatinine and uric acid both show a marked increase. The high figures for those con-

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stituents continue for about 8 days after the injection. Throughout the series of treatments on Dog 1, we find a steady increase in the volume of urine eliminated. At first the amount was 200 cc. and after the treatments it gradually rose to 1 liter."

"On May 8 the animal received a fourth injection of 64 millicuries. This was followed by vomiting and refusal of most of the food for several days. The fact that the third and fourth injections were smaller in quantity than the first, and were followed by marked general effects, shows that the animal failed to recover completely from previous treatments with the emanation. Shortly after the fourth injection the animal was killed and an autopsy made. The autopsy findings will be reported in detail elsewhere."

"The results of injections of active deposit on the bull terrier; uric acid is eliminated only in very minute quantities, hence quantitative determinations of this constituent have been omitted. After a control period of 5 days, Dog 2 received the first injection of 120 millicuries. Urine voided voluntarily 15 minutes after the injection contained 9 millicuries of radio-activity. A decided rise in total nitrogen was noted which reached the maximum figure on the second day. Urea rose proportionately with the total nitrogen and ammonia was decidedly increased. Total phosphates were almost doubled. White cells dropped from about 14,000 to 2,000 after the injection. The bull terrier did not seem to bear the injections so well as the preceding animal for on the third day following this treatment there was vomiting, diarrhea, and refusal of food. Determinations were omitted during this period. This dog also tended to lose weight throughout the experiment. 1 kilo was lost during this period so that creatinine which was high in the control period was considerably lower when the second injection of 17 millicuries was given."

"Probably because of the decided effect produced by the first treatment 3 weeks previously, this small dose caused an appreciable rise in total nitrogen with a proportional increase in urea, ammonia, and creatinine, which was evident for 3 days. Total phosphates were somewhat increased."

"Ten days after the second treatment 54 millicuries were injected. This dose produced no general effect except that the animal refused part of the food on the fourth day. Total nitrogen, urea, and ammonia were considerably increased for 3 days and remained above normal for 10 days. Creatinine was not affected."

"Two weeks later, the last injection of 146 millicuries was given. All food was refused for 4 days, and when on the fifth day more food was eaten severe diarrhea immediately followed. The dog lost 1.5 kilos during this time. She was then anesthetized and an autopsy made."

"Our results record the effect of a purely physical agent, radium emanation, upon the metabolism. The experiment with Dog 1 is the most satisfactory, since in this animal the dosage employed was not great enough to produce general indisposition or sickness."

"In every instance in both experiments the injection of active deposit was followed by an increased output of nitrogen, reaching the maximum figure on the second day after the treatment. Urea fluctuates with the total nitrogen, but the absolute as well as relative amount of the total nitrogen excreted as ammonia nitrogen is decidedly increased, especially on the second day after the treatment."

"Much interest may be attached to the marked increase in crea-



timine which is noted in Dog 1. The quantity of this constituent is usually independent of volume and of total nitrogen."

"Uric acid showed a marked increase both absolutely and relatively following injection of radioactive deposit."

"The effect of the injection seems to be cumulative because the third treatment in Dog 1, only a little larger than the second injection, produced a very marked effect, while the fourth treatment, although smaller than the first, produced nausea."

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Sir Ernest Rutherford, F.R.S. Nuclear Constitution of Atoms. Synopsis of the Bakerian Lecture delivered before the Royal Society on June 3. *Nature*, CV, 500, June 17, 1920.

The idea of the nuclear constitution of atoms was developed from an examination of the scattering of swift alpha-particles in passing through matter, and the advance afterwards made was due to the proof by Moseley of the close connection between the atomic number of an element and the nuclear charge. The accurate determination of the nuclear charge is of prime importance. Recent unpublished experiments by Mr. Chadwick in the Cavendish Laboratory indicate that the nuclear charge on an atom in fundamental units is equal to the atomic number within an accuracy of about 1 per cent. It follows that there is a region surrounding the nucleus where the law of the inverse square holds accurately. The problem of the constitution of the atom divides itself naturally into two parts: One the arrangement of the external electrons on which the ordinary chemical and physical properties of the atom depend, and the other the constitution of the nucleus on which depend the mass of the element, the possibility of isotopes, and radioactivity. The nucleus is composed of positively charged units and negative electrons in very close combination, and estimates of its dimensions are possible from a study of the collision of alpha-particles with light atoms. Close to the nucleus there is a rapid change in the magnitude and direction of the forces, probably in part connected with the deformation of the nucleus structure under the intense forces which arise in a close collision.

Unless the nuclei are very stable, it is to be anticipated that they would be deformed, and possibly broken up, as a result of a direct collision with swift alpha-particles. In previous experiments evidence was given that long-range particles resembling hydrogen atoms were liberated by the passage of alpha-particles through pure nitrogen. New experiments have been made to determine by a modified method the nature of these particles by bending them in a magnetic field. The amount of deflection of the particles liberated from the nitrogen of the air was shown to be the same as for H atoms arising from a mixture of hydrogen and carbon dioxide. This showed definitely that hydrogen is one of the products of the disintegration of the nitrogen atom, and is one of the original components of the nitrogen nucleus. The possibility that the long-range particles are atoms of mass 2, 3 or 4 carrying a single charge may be definitely excluded.

The deflection in a magnetic field of the short-range particles which are liberated from nitrogen and oxygen, and were originally assumed to recoil atoms of these elements, is not only much greater than that to be

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expected for such recoil atoms, but is also greater than the alpha-particle but less than the H atoms liberated from a mixture of hydrogen and carbon dioxide.

There is evidence that these particles are atoms of mass about 3, carrying two charges. Consequently the atom of nitrogen can be disintegrated in two ways by collision with alpha-particles: One by the escape of an H atom, and the other by the expulsion of mass 3, and both processes occur independently. Atoms of mass 3 are also released from oxygen atoms, but H atoms cannot be detected.

It may be concluded, therefore, that atoms of mass 3, carrying two positive charges, are components of the nuclei of nitrogen and oxygen.

This new atom is to be regarded as an isotope of helium, and should give nearly the same spectrum. The energy of motion of the atom of mass 3 expelled from nitrogen and oxygen is about 8 per cent. greater than the original energy of the alpha-particle, showing that energy is liberated as a result of the disintegration. The atoms of mass 3 probably consist of three hydrogen nuclei with one binding electron, and atoms of helium of four hydrogen nuclei and two electrons. Apart from hydrogen itself, these atoms are important secondary units in the building up of atomic nuclei. In the light of the new experimental evidence, examples are given of the possible modes of formation of isotopes and possible structures of nitrogen and oxygen nuclei are considered. It is pointed out that close combinations may exist of H nuclei and electrons, giving rise to atoms of zero nuclear charge, and that such a conception is needed to explain the evolution of the heavy element.

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